REMARKS

Claims 1-69 are currently pending in the application. Claims 1, 3, 5, 47, 50, and 51 are amended. Claims 2, 7-46, 48-49, and 52-69 are withdrawn. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Objection to the Specification

The Office Action states that the specification is objected to because of embedded hyperlinks. Applicants have amended the specification herein to remove the hyperlink on page 62.

Rejection of Claims 50 and 51 Under 35 U.S.C. §112, Second Paragraph

The Office Action states that claims 50 and 51 are rejected under §112, second paragraph for reciting "complementary." The Office Action states that a "complementary" nucleic acid is defined as a sequence that hybridizes specifically to another polynucleotide sequence, but that the definition is vague because it does not set out what the other sequence is. In addition, the Office Action states that "specific hybridization" is vaguely defined as referring to the formation of hybrids between a probe and a specific target. The Office Action states in characterizing the definition of "specific hybridization," that "for example, a probe 'preferentially hybridizes to a specific target so that a single band is observed on Southern blot.'" The Office Action concludes that the definition does not provide a complete a fixed definition for the phrase "specific hybridization" because the disclosure provides "only an example" of what might be encompassed by the phrase.

The question is whether one of skill in the art, reading the claimed invention in light of the specification, would know whether a given antisense oligonucleotide was complementary to the recited mRNA sequence (and, thus, falls under the claim). The specification teaches that the term "complementary to" refers to a sequence that can hybridize specifically to another polynucleotide sequence. The fact that the definition does not specify the identity of the "other sequence" is irrelevant to the question of whether the term "complementary" is definite. The term "complementary" is defined in terms of a generic sequence; that is, a given polynucleotide

sequence is complementary to another polynucleotide sequence that it is able to specifically hybridize to. Thus, there is no need to specify what "the other sequence is" as asserted by the Office Action.

The term "complementary" is well understood in the art. Moreover, the metes and bound of the term as recited in the instant claims, when read in view of the specification is clear and unambiguous. The specification teaches that the term "complementary to" refers to a sequence that can specifically hybridize to another sequence. In addition, the specification does teach that an example of specific hybridization includes where one polynucleotide preferentially hybridizes to another polynucleotide "such that, for example, a single band corresponding to said hybridization can be identified on a Southern blot or a Northern blot of DNA or RNA prepared from a suitable source." The fact that the specification provides an example of a criterion for determining specific hybridization does not mean that the term specific hybridization is unclear, or that the term complementary is vague. For any given antisense oligonucleotide sequence, one of skill in the art, based on the definition in the specification could determine whether the sequence was complementary and, thus, whether it falls under claim 50 or 51. One of skill in the art could determine whether the antisense oligonucleotide specifically hybridized to the recited target mRNA sequence such that a single band corresponding to the hybridization could be identified on a Southern blot, or a Northern blot. The definitions provided in the specification do not merely provide "only an example of what might be encompassed by" the phrase specific hybridization (and, thus, complementary), but instead provide a test that can be used to identify whether a given antisense oligonucleotide is, in fact, complementary to the recited mRNA target. As such, claims 50 and 51 are clear and unambiguous with respect to the term "complementary."

The Office Action also states that claims 50 and 51 are indefinite for the recitation of "corresponding." The Office Action states that "corresponding" is defined in terms of sequences being "complementary" and since complementary is allegedly vague, so too is the term "corresponding." As noted above, however, the term "complementary" is clear and unambiguous. Moreover, the specification teaches at page 22, lines 18-20 that a "corresponding mRNA sequence of SEQ ID No. 1 refers to a mRNA molecule transcribed from a polynucleotide comprising SEQ ID No. 1." Thus, in the context of claim 50, an "mRNA sequence

corresponding to a sequence comprising SEQ ID No. 1 or SEQ ID No. 5" refers to an mRNA molecule transcribed from the polynucleotide sequence of SEQ ID NO: 1 or SEQ ID NO: 5. One of skill in the art, reading the claim in view of the specification, would have a clear and unambiguous understanding of the meaning of "corresponding" as recited in claim 50. Applicants therefore request that the rejections under §112, second paragraph be reconsidered and withdrawn.

Rejection of Claims 1, 3-6, 47, 50, and 51 Under 35 U.S.C. §112, First Paragraph

Written Description

The Office Action states that claims 1, 3-6, 47, 50, and 51 are rejected under §112, first paragraph for alleged lack of written description. The Office Action states that the claims encompass polynucleotides "comprising **a** sequence of SEQ ID NO: 1 or 2," which the Office Action considers to encompass any portion of SEQ ID NO: 1 or 2. The Office Action states that the claims encompass polynucleotides comprising SEQ ID NO: 2, but that the claims do not define the 5' nucleotides flanking SEQ ID NO: 2 or the overall functional activity of the claimed polynucleotide. With respect to claims 50 and 51, the Office Action states that because the terms "complementary" and "corresponding" have not been clearly defined, the claims encompass polynucleotides that share "any level of sequence complementarity" to SEQ ID NO: 1. The Office Action also states that nucleic acids comprising SEQ ID NO: 1 and nucleic acids consisting of SEQ ID NO: 2 meet the written description requirement, but that the specification does not provide written description of the genus of nucleic acids comprising a portion of SEQ ID NO: 1 or 2 or a sequence sharing any level of sequence complementarity with SEQ ID NO: 1 or 2.

To clarify the claimed subject matter, claims 1 and 50 have been amended to recite "comprising the sequence of SEQ ID NO: 1 or SEQ ID NO: 2" (claim 1), or "complementary to the mRNA sequence corresponding to the sequence comprising SEQ ID No. 1" (claim 50). Thus, the claims as amended do not encompass polynucleotides comprising any portion of SEQ ID NO: 1 or 2. With respect to SEQ ID NO: 2, while the Office Action in one instance states that the claims do not define the functional activity of SEQ ID NO: 2, in a second instance, the

Office Action acknowledges that the specification teaches that SEQ ID NO: 2 is a specific fragment of SEQ ID NO:1 that encodes a polypeptide that binds to and inhibits telomerase. Claim 1 recites a polynucleotide comprising the sequence of SEQ ID NO: 1 or a fragment of SEQ ID NO: 1, specified as SEQ ID NO: 2 (thus, SEQ ID NO: 1 is a polynucleotide comprising the sequence of SEQ ID NO: 2). The Office Action does not make clear why one of skill in the art would doubt Applicants' possession of either of the claimed sequences, particularly when the claims specifically recite the sequences by sequence identifier number. In addition, it is no clear why the specification would be deemed to have sufficient written description for a sequence comprising SEQ ID NO: 1, but not for a sequence comprising SEQ ID NO: 2, a fragment of SEQ ID NO: 1. In the even that the Examiner believes that the current rejection should be maintained in light of the current amendments and remarks, Applicants request that the Examiner point out specifically what aspects of the claimed invention Applicants have not put into the possession of one of skill in the art.

With respect to claims 50 and 51, as noted above, the terms complementary and corresponding are clearly defined in the specification. As such, the claims do not encompass antisense oligonucleotides with "any level of sequence complementarity," but instead require that the recited antisense oligonucleotide be complementary as defined in the specification (i.e., at least a be able to produce single band corresponding to said hybridization identifiable on a Southern blot or a Northern blot of DNA or RNA prepared from a suitable source). The use of antisense technology is well known in the art and, moreover, the specification teaches the use of a PinX1 antisense RNA molecule to deplete PinX1 and increase tumorogenicity. Thus, one of skill in the art would have readily appreciated that Applicants were in possession of an antisense oligonucleotide complementary to the mRNA molecule corresponding to the sequence of SEQ ID NO: 1.

In view of the foregoing, Applicants request that the rejections be reconsidered and withdrawn.

Enablement

The Office Action states that claims 1, 3-6, 47, 50, and 51 are rejected because the specification, while being enabling for an isolated polynucleotide comprising SEQ ID NO: 1 and polynucleotides consisting of SEQ ID NO: 2, does not provide enablement for polynucleotides comprising SEQ ID NO: 2 or fragments of SEQ ID NO: 1 or 2. The Office Action analyzed the enablement requirement according to the Wands factors, and Applicants traverse the rejection accordingly.

Breadth of the Claims

As noted above, the claims have been amended to recite "comprising the sequence of SEQ ID NO: 1 or SEQ ID NO: 2" (claim 1), or "complementary to the mRNA sequence corresponding to the sequence comprising SEQ ID No. 1" (claim 50). The Office Action states that the claims do not define the 5' nucleotides that flank the sequence of SEQ ID NO: 2 or the overall functional activity of the claimed polynucleotide. The fact that the claims are silent as to the polynucleotide sequence 5' of the sequence of SEQ ID NO: 2 does not render the claims non-enabled. As the Office Action acknowledges, SEQ ID NO: 2 is a fragment of SEQ ID NO: 1 that encodes a polypeptide that binds to and inhibits telomerase.

With respect to claims 50 and 51, as described above, the terms "complementary" and "corresponding to" are clear and unambiguous, and do not permit a reading of the claims to encompass an antisense oligonucleotide having any degree of complementarity with the mRNA corresponding to SEQ ID NO: 1.

Nature of the Invention

The Office Action states that the claims fall into a class of invention that has been characterized as "the unpredictable arts such as chemistry and biology." Clearly, the biological arts cannot be universally unpredictable, otherwise no patents would issue on biological inventions, because no invention would meet requirements of §112. The instant invention is not unpredictable, and relates to polynucleotide molecules comprising specified sequences, recited in the claims by sequence identifier number.

State of the Art

The Office Action correctly states that the specification teaches the sequence of SEQ ID NO: 1, encoding PinX1 and the sequence of SEQ ID NO: 2 coding for a fragment of PinX1 that comprises the telomerase binding domain. With respect to the Office Action's description of the state of the art for SEQ ID NO: 5, Applicants note that claims drawn to SEQ ID NO: 5 are not part of the elected invention.

Predictability of unpredictability of the art and degree of experimentation

The Office Action states that the prior art acknowledges the unpredictability in modifying the nucleotide sequence of a gene, and that modification of even a single nucleotide within a coding or non-coding sequence can significantly alter the functional properties of that gene. The Office Action states that while the specification teaches that the C-terminal domain of PinX1 is important for telomerase binding activity, the specification does not teach "any particular amino acids therein which are critical for maintaining binding activity and does not teach any particular nucleotides within the full length PinX1 polynucleotide which encode for amino acids that are critical for other functional activities." The Office Action concludes that it is unpredictable "as to how modifying sequences within SEQ ID NO: 1 will effect the overall functional properties of the resulting gene...[or] how adding nucleotides of any identity or length to the terminus of SEQ ID NO: 2...will effect the functional properties of the resulting nucleic acid and encoded polypeptide.

The instant claims have been amended to recite "comprising the sequence of SEQ ID NO: 1 or SEQ ID NO: 2" (claim 1), or "complementary to the mRNA sequence corresponding to the sequence comprising SEQ ID No. 1" (claim 50), and thus, no longer recite polynucleotides comprising **a** sequence of SEQ ID NO: 1 or 2. As amended, the claims relate to a polynucleotide comprising all of either SEQ ID NO: 1 or SEQ ID NO: 2, thus, the issue of predictability as to what sequences within SEQ ID NO: 1 or 2 can be modified is moot with respect to the enablement analysis. With respect to the assertion by the Office Action that the specification does not teach particular amino acids encoded by SEQ ID NO: 2 that are critical for maintaining telomerase binding activity, again, this point is moot as the claims recite a polynucleotide comprising the sequence of SEQ ID NO: 2, and not sub-sequences thereof.

With respect to the assertion that the specification does not provide guidance as to how adding nucleotides of any identity or length to the terminus of SEQ ID NO: 2 will effect the functional properties of the encoded polypeptide, Applicants submit that the claims are enabled as currently written. Claim 1 and its dependents recite a polynucleotide comprising the sequence of SEQ ID NO: 2. The specification teaches that SEQ ID NO: 2 encodes the 74 C-terminal amino acid residues of PinX1 that are required for binding to Pin2/TRF1 (page 66). The specification teaches at page 42-51 how one of skill in the art would determine telomerase function and activity. Thus, if one of skill in the art desired to add additional nucleotides to the sequence of SEQ ID NO: 2 (taught as encoding the critical amino acid residues for telomerase binding and inhibition), they could do so and then follow the teachings of the specification to determine whether the additional residues altered the function of the polypeptide encoded by SEQ ID NO: 2. Such testing is merely routine and does not amount to undue experimentation. Thus, the specification teaches one of skill in the art how to make and use a polynucleotide comprising the sequence of SEQ ID NO:2. With respect to the SEQ ID NO: 1, the Office Action admits that the specification is enabling for a polynucleotide sequence comprising SEQ ID NO: 1 as presently claimed.

Amount of Direction/Guidance and Presence of Working Examples

The Office Action states that the specification does not provide guidance as to how to predictably make and use nucleic acids comprising any portion of SEQ ID NO: 1 or 2, flanked by nucleotides of any length and identity. The Office Action also states that the specification only teaches the sequence of SEQ ID NO:1 and a fragment thereof, SEQ ID NO: 2. The Office Action concludes that the specification does not provide working examples of how to predictably make and use nucleic acids comprising SEQ ID NO: 2. Applicants respectfully traverse the rejection.

As noted above, the claims have been amended to recite a polynucleotide "comprising the sequence of SEQ ID NO: 1 or SEQ ID NO: 2" (claim 1), or antisense oligonucleotide "complementary to the mRNA sequence corresponding to the sequence comprising SEQ ID No. 1" (claim 50). As such, the claims do not encompass "any portion" of SEQ ID NO: 1 or 2. The

methods for making nucleic acids are routine in the art, thus, the specification need not expressly teach how to make a nucleic acid comprising SEQ ID NO: 2 because one of skill in the art, given the sequence of SEQ ID NO: 2, would know how to add additional nucleotides, if desired, to the 5' end. In addition, the specification, in teaching the sequence of SEQ ID NO: 1, provides a working example of a polynucleotide sequence comprising the sequence of SEQ ID NO: 2. The polynucleotides encompassed by the claims can be readily envisioned, prepared, and characterized by one of ordinary skill in the art according to the methods taught in the specification without having to resort to undue experimentation.

When considered together, the amended claims and teachings of the specification provide ample guidance to permit one of skill in the art to practice the claimed invention without undue experimentation. That is, one of skill in the art could readily make and use a polynucleotide sequence comprising the sequence of SEQ ID NO: 1 or SEQ ID NO: 2 without undue experimentation. Accordingly, Applicants request that the rejection for lack of enablement be reconsidered and withdrawn.

Rejection of Claims 1, 3-6, 50 and 51 Under 35 U.S.C. §102

Liao et al.

The Office Action states that claims 1, 3-6, 50 and 51 are rejected as anticipated by Liao et a. (Hepatology and GenBank entry). The Office Action states that Liao et al. teaches a nucleic acid sequence having 59% identity with nucleotides 19-1302 of SEQ ID NO: 1 and thus anticipates the claimed invention.

As amended, the instant claims recite a polynucleotide sequence comprising the sequence of SEQ ID NO: 1 or SEQ ID NO: 2, meaning that to anticipate, a prior art reference must teach the whole sequence of SEQ ID NO: 1 or SEQ ID NO: 2. As stated by the Office Action, Liao et al. teaches a sequence having only 59% identity to only a portion of the sequence of SEQ ID NO: 1 (the Liao et al. sequence similarly lacks complete identity with the sequence of SEQ ID NO: 2). Liao et al., therefore, does not teach a polynucleotide comprising the sequence of SEQ

ID NO: 1 or SEQ ID NO: 2. Liao et al. does not anticipate the claimed invention, and Applicants request that the rejection be reconsidered and withdrawn.

Hillman et al.

The Office Action states that claims 1, 3-6, 50 and 51 are rejected as anticipated by Hillman et al. The Office Action states that Hillman et al. teaches a polynucleotide sequence having 99% sequence identity with a portion of SEQ ID NO: 1 and 2. The sequence disclosed by Hillman et al., however, does not have complete identity with either the sequence of SEQ ID NO: 1 or 2 and, thus, Hillman et al. does not teach a polynucleotide comprising the sequence of SEQ ID NO: 1 or SEQ ID NO: 2. Accordingly, Hillman et al. does not anticipate the claimed invention and Applicants request that the rejection be reconsidered and withdrawn.

Rejection of Claims 5 and 6 Under 35 U.S.C. §103(a)

The Office Action states that claims 5 and 6 are unpatentable over Liao et al. in view of Hillman et al. with respect to the labeling of the claimed polynucleotide. Regardless of the teachings in either reference, neither reference teaches a polynucleotide sequence comprising the sequence of SEQ ID NO: 1 or 2. Because a finding of obviousness requires that the cited prior art, considered alone or together, teach each element of the claimed invention, the combined teachings of Liao et al. and Hillman et al. do not obviate claims 5 and 6 because they fail to teach the base invention of claim 1. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

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